Achieving the Desired State: FDA's Critical Path Introduction A CBER Perspective

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Vision for CBER

Innovative Technology
Advancing Public Health

Protect and improve public and individual health in the US, and if possible, globally

Facilitate development, approval and access to safe and effective products

Strengthen CBER as preeminent regulatory Agency for biologics

How is CBER Unique?

The Science of Biologics Product Evaluation

- **CBER guidance based on science can foster innovation and improve chances of success of entire field of biological products**
- **CBER scientists are part of the review process *during* product development—they directly see the successes, failures, and missed opportunities due to lack of science**
- **CBER can play both a direct role as well as a convening and coordinating role for scientific needs across sponsors**

Defining the Critical Path

Accelerating the Development of Medical Products

- A scientific process through which a potential human drug, biological product, or medical device is transformed from a discovery or "proof of concept" into a medical product.

- Modernize the techniques and methods – “tools” used to evaluate the safety, efficacy and quality of medical products as they move from product selection and design to mass manufacture.

What is CBER doing to improve the Product Development Process ?

- Working with stakeholders to develop and prioritize needs
- Coordinating and collaborating with academic and industry scientists to respond to these needs
  - Workshops & guidances
- Applying new science to chart a more predictable and efficient path for new biologics product evaluation
- Routinely assessing progress and revising priorities with stakeholders

Better Product Development Toolkits are Needed

- Tools for Assessing Safety
- Tools for Demonstrating Medical Utility (Effectiveness or Benefit)
- Tools for Characterization & Manufacturing

Towards a Better Toolkit for Demonstrating Safety & Effectiveness through Good Clinical Practice

Towards a Better Manufacturing Toolkit through the Right Manufacturing Standards

Efforts for Better Toolkits led by CBER's Office of Compliance & Biologics Quality (OCBQ)

- OCBQ Product Development-Related Responsibilities
- Good Clinical Practice/Design
- Manufacturing Science
- Cross-Cut Among all Products

Related OCBQ Responsibilities

- IND reviews
- Clinical investigation oversight
- BLA reviews
- CMC expertise
- Manufacturing change reviews
- Pre-approval and manufacturing change inspections

Opportunities Through OCBQ in Critical Path

- Manufacturing science and clinical trial design planning
  - as part of pre-IND, pre-IDE, and pre-BLA process
- Expert guidance
- Facilitate effective transition from R&D stage to clinical stage to product development stage

Critical Path To New Product Development

- **Expanded and early IND, IDE, and BLA guidance/discussion to facilitate --**
  - **Innovative science-based practices**
  - **Clear path to product approval**
  - **Efficient and effective commercial-scale manufacturing**
  - **Safe and effective products for patients**
  - **Increase in critical medical product availability**
  - **Avoiding regulatory problems later in development and distribution process**

CBER Sponsors/Manufacturers

Range of Experience

- **Established drug/biologic companies**
- **New product or new facility development at established or licensed companies**
- **Small-scale manufacturers**
- **Start-ups, academia, and individuals**
  - **Limited experience**
  - **Limited resources**

Good Clinical Practice/Design

- Clinical studies needed to show new product safe and effective
- Rights, safety, and welfare of subjects in clinical trials paramount
- Quality/usefulness of clinical data critical to product approval
- Often new trials and new sponsors, sponsor-investigators, and investigators in cutting edge areas (e.g., cell and gene therapies)

Good Clinical Practice/Design

- Early dialogue in early stages of clinical trial design will facilitate:
  - Effective movement from research phase into clinical trial phase
  - Choice and training of qualified clinical investigators
  - Identification and development of monitoring responsibilities and trial monitoring plan
  - Selecting monitors
  - Role of IRB
  - Quality oversight of product manufacturing

Good Clinical Practice/Design

How to Protect Subjects and Provide Quality Data

- **Available guidance includes "ICH E6: Good Clinical Practice: Consolidated Guidance"**
- **Regulations (21 CFR 50, 56, 312, & 812)**
- **Quality management principles**

Manufacturing Science

- Efficient and effective manufacturing science design and control activities critical to product safety, effectiveness, and availability

- Consider early in the development process

Manufacturing Science

Providing Safe and Effective Products

- **Very useful information in FDA Manufacturing Guidance documents**

  For example:

  Sterile Drug Products Produced by Aseptic Processing

  www.fda.gov/cber/gdlns/steraseptic.pdf

  Also refers to other guidance documents

- **Regulations (21 CFR 210-11, 600, 606, 610, 820)**

Manufacturing Science

- Build quality into product development process
- Choose acceptance criteria wisely
  - Based on data
  - Based on intended process
- Robust system/process critical
- Absence of planning and implementation of manufacturing science principles into development process can impact product integrity and delay product approval

Manufacturing Science
Examples

- **Early discussion will be beneficial when considering novel approaches to:**
  - **Scale-up facility design**
  - **Equipment qualification**
    - » **Sampling techniques**
    - » **Control of manufacturing processes**
    - » **Compliance with cGMPs during product development and manufacturing stages**

Manufacturing Science

Examples

- **OCBQ can provide guidance to facilitate decisions impacting final product quality:**
  - **Product delivery (liquid/lyophilized/device /etc.)**
  - **Container/closure system**
  - **Raw materials**
  - **Manufacturing process**
  - **Sampling/testing**
  - **Logistics (manufacturing site/shipping of product)**
  - **Technology transfer**
  - **Scale-up**
  - **Automation**

Summary

- Early, informed, and effective planning
- Communication – within company and with FDA
- Integration of trial design and manufacturing science issues into early development plan
- Facilitates innovation, quality science/data, new product development
- Can reduce development costs, improve likelihood of success during clinical trial and manufacturing phases
- Can expedite licensing process/approval

Summary
continued

- **Work together to provide patients with safe and effective products, and to increase product availability**

- **We look forward to discussing these issues today and working with you in the critical path to new product development**

CBER Critical Path Opportunities beyond Compliance and Manufacturing

- New vaccine delivery systems, rapid use vectors, adjuvants, including vaccines for BT, EID
- Develop and make available well characterized cell banks (and related methods to assay for safety/adventitious agents) useful for vaccine and other biologics production
- Improve longevity/storage of blood and tissues

More CBER Critical Path Opportunities

- Characterize cell therapies & link this information to standardized outcomes (e.g. stem cells)

- Develop and evaluate methods for:
  - –Multipathogen, rapid detection of microbial contamination of biologics including blood and tissue products
  - –Pathogen inactivation for blood, plasma, tissues and other products

Continuing the collaborative process
The Path Forward

- Continue open discussions of Biologics Critical Path issues
  - Develop CBER science future priorities and agenda
  - Seek outside scientists for consultation, collaborative projects or to inspire for independent projects

Continuing the collaborative process
The Path Forward

Continued

- **Transparency and accountability**
  - **CBER science organization, priorities and outcomes to be presented publicly in 2005**
  - **Continue regular formal external reviews of CBER science programs to seek evaluation of quality and to update priorities**

We're Here to Help You!

www.fda.gov/cber

www.fda.gov/oc/initiatives/criticalpath

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